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POTENTIAL OF GINGER (Zingiber O. Rosc) EXTRACT IN *PORPHYROMONAS GINGIVALIS ATCC®33277™* CAUSES OF PERIODONTITIS (In vitro)

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Abstrak

Bakteri Porphyromonas gingivalis merupakan salah satu patogen yang dapat menyebabkan periodontitis, suatu infeksi destruktif pada jaringan periodontal. Periodontitis kronis diobati dengan obat kumur klorheksidin 0,2%, namun juga mengubah rasa, warna gigi dan punggung lidah, meningkatkan kalkulus, mengeringkan mukosa, dan menyebabkan mulut berbau. Jahe alternatif (Zingiber O. Rosc) berupa fenol, minyak atsiri, flavonoid, dan terpenoid, memiliki senyawa antimikroba yang berfungsi mengubah sifat protein sel bakteri, mengganggu perkembangan dinding sel, melepaskan transduksi energi, dan menghambat proses yang menyebabkan bakteri. kematian sel. Tujuan penelitian adalah untuk mengetahui Konsentrasi Hambat Minimum (KHM), Konsentrasi Bakterisida Minimum (MBC) dan Zona Hambat ekstrak jahe pada Porphyromonas gingivalis ATCC®33277™ konsentrasi 60%, 40%, 20% dan 10%. Metode yang digunakan adalah eksperimen laboratorium, dengan desain Posttest Only Control Group Design. sedangkan zona hambat diukur dengan jangka sorong digital dan metode difusi pada blank disk. Jahe diekstraksi dengan metode maserasi, dikelompokkan menjadi 6 perlakuan dengan kelipatan konsentrasi 4 kali pengulangan, menggunakan uji Oneway Anova yang dilanjutkan dengan uji Post Hoc Least Significance Different (LSD) untuk mengetahui perbedaan nyata. Hasilnya, zona hambat dengan konsentrasi 60%, 40%, 20%, dan 10% mempunyai diameter rata-rata berturut-turut sebesar 22,87mm, 18,5mm, 14,5mm, dan 11,31mm, serta nilai MIC sebesar 10% dan 40. % MBC, zona hambat tertinggi adalah 60%. Kesimpulannya, konsentrasi yang lebih besar akan lebih efisien dalam mencegah perkembangan Porphyromonas gingivalis ATCC®33277TM.

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***Kata kunci**: Porphyromonas gingivalis ATCC®33277™; Ekstrak Jahe; Konsentrasi Penghambatan Minimum; Konsentrasi Pembunuhan Minimum; Zona Penghambatan.*

***Keywords**: Porphyromonas gingivalis ATCC®33277™; Ginger Extract; Minimum Inhibitory Concentration; Minimum Killing Concentration; Zone of Inhibition.*

Abstract

The bacterium Porphyromonas gingivalis is one of the pathogens that can cause periodontitis, a destructive infection of the periodontal tissues. Chronic periodontitis is treated with 0.2% chlorhexidine mouthwash, however it also changes taste, the color of the teeth and dorsal tongue, increases calculus, dries out the mucosa, and causes the mouth to smell. Alternative ginger (Zingiber O. Rosc) in the form of phenols, essential oils, flavonoids, and terpenoids, has antimicrobial compounds that work to denature bacterial cell proteins, disrupt the development of cell walls, release energy transduction, and block processes that lead to cell death. Purpose of the study is to determine the Minimum Inhibitory Concentration (MIC), Minimum Bactericidal Concentration (MBC) and Inhibition Zone of ginger extract in Porphyromonas gingivalis ATCC®33277™ concentrations of 60%, 40%, 20% and 10%. Method an experimental laboratory, with a

Posttest Only Control Group Design. while the inhibition zone was measured with digital slide calipers and the diffusion method on a blank disk. Ginger was extracted by maceration method, grouped into 6 treatments with multiple concentrations of 4 repetitions, using the Oneway Anova test followed by the Post Hoc Least Significance Different (LSD) test to find out a significant difference. Result, the inhibition zones with concentrations of 60%, 40%, 20%, and 10% had an average diameter of 22.87mm, 18.5mm, 14.5mm, and 11.31mm, respectively, as well as MIC values of 10% and 40% MBC, the highest inhibition zone is 60%. Conclution, greater concentrations being more efficient at preventing the development of Porphyromonas gingivalis ATCC®33277TM.

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INTRODUCTION

Ginger (*Zingiber o. Rosc*.) is a spice plant commonly used as an ingredient in food and drinks all over the world. Ginger has been shown to have antibacterial, anti-inflammatory, analgesic, and antipyretic properties in earlier researches (Alrazhi, Diab, Essa, & Ahmed, 2014),(Sari K, Periadnadi, & Nasir N, 2013),(Indiarto, Subroto, Angeline, & Selly, 2021),(Munda, Dutta, Haldar, & Lal, 2018). According to Mishra's research, ginger contains secondary metabolite components such as phenols, essential oils, flavonoids, and terpenoids that can prevent the growth of bacteria that cause periodontitis and even kill them (Arifiana & Prandita, 2019),(*Riskesdas. Laporan nasional riset kesehatan dasar 2018. Badan Penelitian dan Pengembangan Kesehatan. 2019*, n.d.),(Mishra, Kumar, & Kumar, 2018).

The leaves contain the highest phenol chemicals, and hydroxyl groups (-OH) and alkoxy groups have antioxidant properties (-OR). Because all metabolic activity in bacterial cells are performed by enzymes, which are proteins, phenolic chemicals destroy bacterial cells by denaturing bacterial cell proteins. This causes all metabolic processes in bacterial cells to stop (Nurjanah & Fathia, 2017),(Sari & Nasuha, 2021),(Lestari, Mahmudati, Sukarsono, Nurwidodo, & Husamah, 2018).

Etheric oils or flying oils are other names for essential oils. Essential oils can be used as local anesthetics at high concentrations to treat diseases through aromatherapy (Kurniasari, Hartati, Ratnani, & Sumantri, 2008b),(Kurniasari, Hartati, Ratnani, & Sumantri, 2008a).

Flavonoids have the ability to denature proteins, which are crucial components of bacterial structure. They can also lessen the surface tension of the cell wall, which slows cell development and prevents colonization. Nucleic acid synthesis, cell membrane activity, and energy metabolism are all inhibited by flavonoids. Flavonoids work as an antibacterial by a mechanism that damages the bacterial cell membrane and releases intracellular compounds that combine with extracellular proteins to form complex compounds that cause the bacterial cell to lyse. As a result of interactions with bacterial DNA, flavonoids release transduction energy into the cytoplasmic membrane of bacteria

(Anggraini, Nisa, Da, & Ma, 2019),(Nor, Indriarini, Marten, & Koamesah, 2018),(Nurul dkk., 2020).

Terpenoids are triterpenoid chemicals with strong pharmacological action, including antibacterial, antiviral, anti-inflammatory, cholesterol synthesis inhibition, and anticancer properties. Terpenoid compounds' mode of action as antibacterial agents involves lipophilic compounds damaging membranes, reacting with porins (transmembrane proteins) on the outer membrane of the bacterial cell wall, forming strong polymer bonds and destroying porins, and reducing the permeability of the bacterial cell wall so that the bacterial cells lack nutrition, growth is inhibited, or bacteria are killed (Nasution, 2017),(Nola, Putri, Malik, & Andriani, 2021).

Taxonomy dan Overview

Position of the ginger plant in the systematics (taxonomy) is as follows:(Handayani, 2013)

Kingdom : *Plantae*
Division : *Spermatophyta*
Sub-division : *Angiospermae*
Class : *Monocotyledoneae*
Order : *Zingiberales*
Family : *Zingiberaceae*
Subfamily : *Zingiberoidae*
Genus : *Zingiber*
Species : *Zingiber officinale Roscoe*

Image 1. White ginger (Documentation)

Ginger Uses (*Zingiber o. Rosc*) The active ingredients in rhizomes have a variety of pharmacological effects, including carminative drugs, stimulants for the intestinal gastro tract, antispasmodic, digestive, vasodilator, cough medicine, bronchodilator, analgesic, resolve digestive problems, increase the activity of various intestinal enzymes, pain relief and anti-inflammatory in rheumatism patients, and stimulates blood circulation.

According to Alibasyah's research, ginger extract displayed antibacterial ability against *Porphyromonas gingivalis* at concentrations of 6.25 percent, 12.5%, 25%, 50%, and 100%. The average diameter of the inhibition zone was 10.6 mm, 12.6 mm, 15.6 mm, 20.26 mm, and 28.6 mm (Alrazhi dkk., 2014),(Pairul, Susianti, & Nasution, 2017),(Kholilah & Bayu, 2019),(Alibasyah dkk., 2016).

The periodontal tissues that causes tooth loss and mobility caused by certain microbes, like as *Porphyromonas gingivalis* (Andriani & Chairunnisa, 2019),(How, Song, & Chan, 2016),(Mahalakshmi, Krishnan, Chandrasekaran, Panishankar, & Subashini, 2012),(Harsas dkk., 2021),(Kusuma, Azizah, & Utami, 2021).

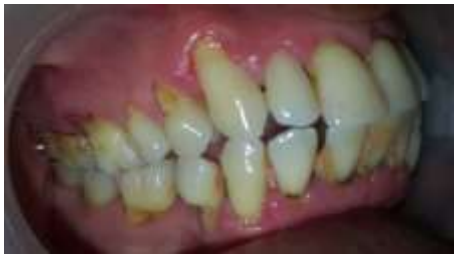


Image 2. Chronic periodontitis(Andriani & Chairunnisa, 2019)

These opportunistic bacterial antigens cause between 40 and 100 percent of instances of periodontitis. 85.75% of these bacteria were discovered in the subgingival plaque associated with chronic periodontitis (Putri CF 2020). The primary characteristics of *Porphyromonas gingivalis* include producing black pigments and being a gram-negative, rod-shaped, non-motile, anaerobic, assacharolytic bacteria (Zhou, Xuedong; Li, 2015),(Putri & Bachtiar, 2020).

Taxonomically, these bacteria are classified as follows:

Kingdom : *Bacteria*
Filum : *Bacterioedetes*
Kelas : *Bacterioedes*
Ordo : *Bacteriodales*
Familia : *Porphyromonadaceae*
Genus : *Porphyromonas*
Spesies : *Porphyromonas gingivalis*

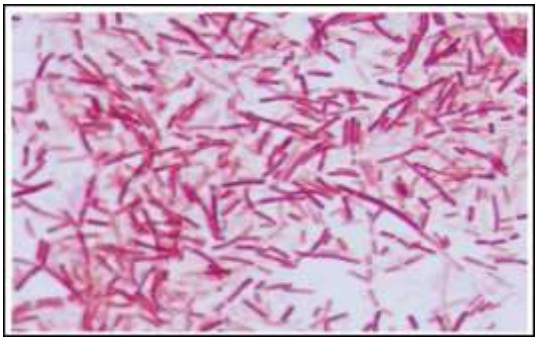


Image 3. *P. gingivalis* (Documentation)

Image 4. *Porphyromonas Gingivalis* bacterial subculture (Documentation)

Measurement of *Porphyromonas Gingivalis* Activity

1. Dilution Method

   The dilution method is one of the methods used to determine the potential of a compound for microbial activity by determining the Minimum Inhibitory Concentration (MIC), Minimum Inhibitory Concentration (MIC) of ginger extract on *Porphyromonas gingivalis* ATCC® 33277™ (Jawetz, Melinick, & Aldeberg, 2004),(KUSMIYATI & AGUSTINI, 2006).

2. Diffusion method

   The disc diffusion method or Kirby-Bauer test is a method often used to determine the inhibition zone of *Porphyromonas gingivalis* ATCC®33277™ from ginger extract. The principle of the diffusion method is carried out by placing a blank disc containing an antibacterial agent on agar media that has been planted with microorganisms, then incubating it at 37°C for 24 hours (Jawetz dkk., 2004),(Kusmiyati & Agustini, 2006).

METHOD

This research used an experimental laboratory with a posttest only control group design, with measurements after all treatments were completed. Ginger extract was made at the Medicinal Plant Research and Development Laboratory (ASPETRI) on Setia Budi Tasbi Complex 2 Block VI no.57 Medan. Bacterial sampling, planting, sample testing for MIC and MBC and inhibition zones were carried out at the Microbiology Laboratory, University of North Sumatra Hospital (USU Hospital).

In calculating the size of the experimental research sample used the Federer formula. Federer's formula:

$(t-1)(r-1) \geq 15$

$(6-1)(r-1) \geq 15$

$5(r-1) \geq 15$

$5r-5 \geq 15$

$r \geq 4$

Description:

t = no. of treatment groups

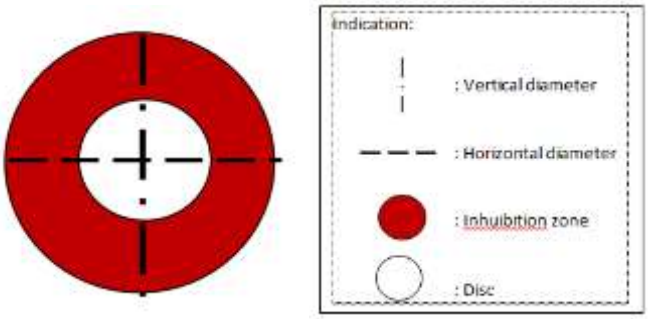
r = no. of replications

In this study, 6 treatment groups were used, namely:

1. Group I : Ginger extract 60%
2. Group II : Ginger extract 40%
3. Group III : Ginger extract 20%
4. Group IV : Ginger extract 10%
5. Group V : Positive control with 0.2% Chlorhexidine (comparison group)
6. Group VI : Negative control using Dimethyl sulfoxide (DMSO) (comparison group)

The number of samples required is 24. In order to obtain the best average results and prevent bias, there were 4 trials for each concentration of ginger extract with *Porphyromonas gingivalis* ATCC®33277TM culture. As a comparison with each concentration of ginger extract, the positive control of 0.2% chlorhexidine and the negative control of DMSO were examined.

Measuring the Inhibition Zone



Measuring Method

$$\text{Diameter zona hambat} = \frac{\phi\text{horizontal} + \phi\text{vertikal}}{2}$$

a) Simplicia

A collection of 1 kg of white ginger that has been obtained. North Sumatra's Raya District, in Simalungun Regency, is where ginger is grown. Ginger is cleaned, diced, weighed at one kilogram, dried, and finally crushed.

Image 5. Ginger that has been cut and cleaned is then put into the drying cabinet

b) Process of manufacturing extract

Weighing 0.2 grams of ginger extract powder, it was then put in a jar and sealed. Afterwards, 2 liters of 96% ethanol were added, agitated for 6 hours, and let to stand for 18 hours. After that, the filtrate was caught using Whatman filter paper No 1. Once the subsequent macerate was obtained, the extraction procedure was repeated using 1 liter of residues mixed with 96% ethanol. Moreover, a container is used to combine the two maserates. At 40 °C, the combined maserate is evaporated in the evaporator. Put in a measuring cup after stirring to achieve a thick extract.

The following formula was used to dilute ginger extract at concentrations of 60%, 40%, 20%, and 10%:

Extract Amount = concentration x 10 ml

1. A 60% concentration of ginger extract solution

To make a volume of 10 ml, weigh 6 ml of ginger extract and dilution it with DMSO. After that, pour it into a beaker glass and mix it to ensure even distribution. After that, place it in a vial marked "60%."

2. A 40% concentration of ginger extract solution
   To make a volume of 10 ml, weigh 4 ml of ginger extract and dilution it with DMSO. After that, pour it into a beaker glass and mix it to ensure even distribution. then place it in a bottle marked "40%."
3. A 20% concentration of ginger extract solution
   To make a volume of 10 ml, weigh 2 ml of ginger extract and dilution it with DMSO. After that, pour it into a beaker glass and mix it to ensure even distribution. After that, place it in a vial marked "20%."
4. A 10% concentration of ginger extract solution
   To make 10 ml, weigh 1 ml of ginger extract and dilute it with DMSO. After that, pour it into a beaker glass and mix it to ensure even distribution. After that, place it in a vial marked "10%."

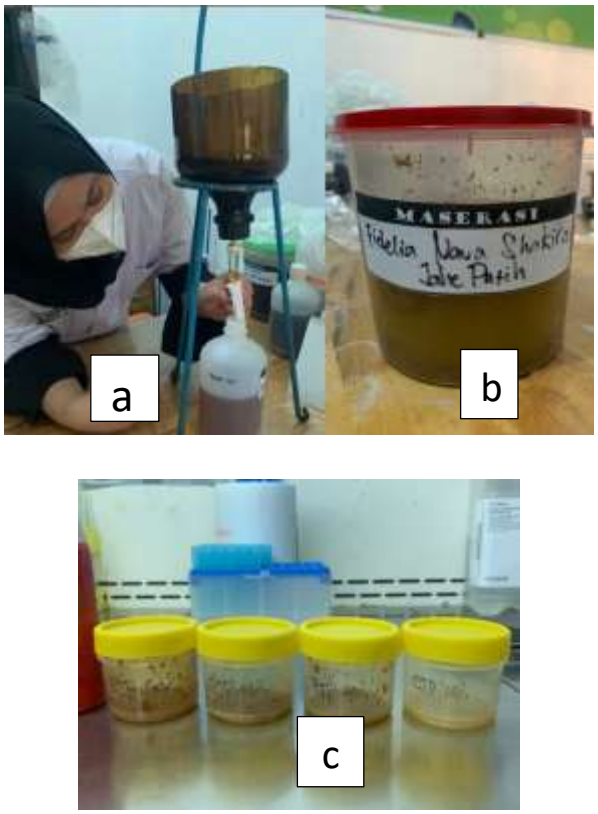


Image 6. A) Ginger extracting process; B) Maceration process of ginger; C) Ginger extract divided into 60%, 40%, 20% and 10% (Documentation)

While making Brain Heart Infusion Broth (BHI-B) Transport Media, 37 grams of BHI-B powder are weighed out and then dissolved in 1L of distilled water. The mixture was then heated using a hot plate and magnetic stirrer until all the ingredients had completely dissolved, and it was then sterilized for 15 minutes at 121°C in an autoclave. Pour 8 ml into each test tube after the media reaches a temperature of 40–45°C.

The preparation of 5% Brucella Agar Sheep Blood Media was carried out at the Microbiology Laboratory of the University of North Sumatra Hospital (USU Hospital) by weighing 45 grams of brucella agar base powder and then dissolving

it in 1L of pure water/distilled water. Furthermore, a hot plate and a magnetic stirrer are used to heat it. then 15 minutes at 121°C in the autoclave. Moreover, Vitox supplement and 5% sheep blood were added once the media had attained a temperature of 40–45°C. The mixture was then homogenized, and based on the quantity of treatments and repetitions, as much as 15 ml was added to each sterile petri dish.

RESULTS AND DISCUSSION

Observation of MIC and MBC Ginger Extract on *Porphyromonas gingivalis* ATCC®33277™

Determination of MIC and MBC to determine the smallest extract concentration that can inhibit the growth/kill bacteria. After being incubated for 24 hours at a temperature of 37°C, the MIC and MBC values of *Porphyromonas gingivalis* ATCC®33277™ were observed by taking a look at the turbidity level in each tube. (Table 1)

Table 1. Turbidity level of ginger extract against *Porphyromonas gingivalis* ATCC®33277™.

Group	Replication			
	I	II	III	IV
60%	+	+	+	+
40%	+	+	+	+
20%	+	+	+	+
10%	+	+	+	+
Klorheksidin 0,2%	-	-	-	-
DMSO	+	+	+	+

Description: + = cloudy; - = clear (not cloudy)

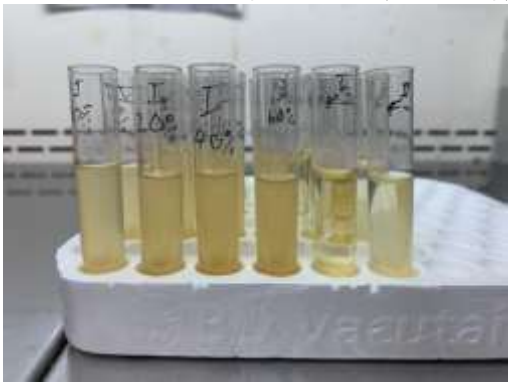


Image 7. MIC and MBC test results of ginger leaf extract against *Porphyromonas gingivalis* ATCC®33277™ bacteria

Proceed to the subculture stage using 5% Brucella Agar Sheep Blood media to determine the MIC and MBC values based on observations of all the 60%, 40%, 20%, and 10% extract tubes that were cloudy because they were influenced by the concentrated color of the extract at a high concentration. The clear tube in the positive control dilution tube, however, demonstrated that *Porphyromonas gingivalis* ATCC®33277™ was successfully eradicated by 0.2% chlorhexidine. The negative control tube for DMSO was cloudy, showing that the substance was ineffective at killing *Porphyromonas gingivalis* ATCC®33277™.

Table 2. The results of calculating the number of *Porphyromonas gingivalis* ATCC®33277™ colonies from culturing the test solution.

Group	Number of Bacterial Colonies (CFU/ml)				
	Replication				Average±SD
	I	II	III	IV	
60%	0	0	0	0	0
40%	0	0	0	0	0
20%	17	39	33	27	29±9,3
10%	166	182	141	196	171±23,5
Klorheksidin 0,2%	0	0	0	0	0
DMSO	≥300	≥300	≥300	≥300	≥300

Based on the results of the subculture of the dilution tube of the positive control, was not found any bacterial growth (0 CFU/ml), while the negative control found bacterial growth (> 300 CFU/ml) and it can be concluded that the MIC value was 10% and the MBC was 40%. The positive control proved to be effective in killing *Porphyromonas gingivalis* ATCC®33277™ bacteria.

Inhibition Zone of Ginger Extract (Zingiber O. Rosc) on the Growth of *Porphyromonas gingivalis* ATCC®33277™ using the Diffusion Method

Using 5% Brucella Agar Sheep Blood as the substrate, the diffusion technique tries to determine the inhibitory zone. Using sterile tips, a suspension of *Porphyromonas gingivalis* ATCC®33277™ bacteria was equally spread over Brucella Agar Sheep Blood media. After incubation, the inhibition zones were then analyzed for. A blank disc containing ginger extract was adhered to the 5% Brucella Agar Sheep Blood surface, incubated for 24 hours, and then observed. Four times were given for each material, and observations were taken of all groups simultaneously. It is demonstrated that there was an inhibitory process for the test material against *Porphyromonas gingivalis* ATCC®33277™ by the establishment of a clear zone on solid medium in the blank disc area. The diameter of the inhibition zone was measured using a slide caliper (Table 3).

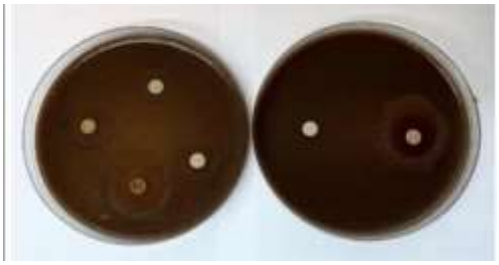


Image 8. Results of the inhibition zone diameter of *Porphyromonas gingivalis* ATCC®33277™ using the diffusion method. (Documentation)

Table 3. Average inhibition zones of several concentrations of ginger extract against *Porphyromonas gingivalis* ATCC®33277™

Group	Diameter of Inhibition Zone (mm)				
	Repetition				Average±SD
	I	II	III	IV	
60%	23,5	22,5	22.5	23	22,87±0,47
40%	18,5	19	18,5	18	18,5±0,40
20%	14	14,5	15	14,5	14,5±0,40

Group	Diameter of Inhibition Zone (mm)				
	Repetition				Average±SD
	I	II	III	IV	
10%	11,25	11,5	11	11,5	11,31±0,23
Klorheksidin 0,2%	29,5	30	31	29,5	30±0,70
DMSO	0	0	0	0	0

Description: 0 = no inhibition

Results showed that the average diameter of the ginger extract's (*Zingiber O. Rosc*) inhibitory zone on *Porphyromonas gingivalis ATCC®33277™ growth was 22.87 mm, 18.5 mm, 14.5 mm, and 11.31mm, respectively. Ginger extract (Zingiber O. Rosc) inhibits Porphyromonas gingivalis ATCC®33277™ at all doses.*

This study proves that ginger extract (*Zingiber officinale Roscoe*) has potential antibacterial effectiveness on *Porphyromonas gingivalis* ATCC®33277™. Ginger extract (*Zingiber officinale Roscoe*) can inhibit growth at a concentration of 10% with an average number of colonies of 171 CFU/mL. and kills *Porphyromonas gingivalis* ATCC®33277™ at a concentration of 40% with an average colony count of 0 CFU/mL. According to Davis and Stout's criteria for antibacterial power, the diffusion method results showed the largest average diameter of the inhibition zone at a concentration of 60% with an average diameter of 22.87 mm. This diameter of the inhibition zone was classified as strong with a range of 10-20 mm. This demonstrates the antibacterial properties of ginger extract (*Zingiber officinale Roscoe*).

This is comparable to Alibasyah's research, which demonstrated that ginger already had a clean zone with an average diameter of 10.6 mm at a concentration of 6.25%, indicating that antibacterial action had taken place. [10]

The study by Mirsha et al. demonstrated how ginger (*Zingiber O. Rosc*) and its phenolic components, such gingerol, can act as antibacterials in periodontal disease. (Mishra dkk., 2018). Streptococcus mutans was tested in Sriwidasari's study employing ginger extract (*Zingiber O. Rosc*), which formed an inhibitory zone at a dose of 6.25 mg/ml and demonstrated antibacterial activity (Sari K dkk., 2013).

The essential oils and flavonoids found in temulawak (*Curcuma xanthorrhiza*) and citronella (*Cymbopogon nardus*) have been shown by Hasibuan SY's research to have antibacterial properties on Streptococcus Mutans bacterium. It was discovered that 20% Temulawak extract had a moderate inhibitory response whereas 20% citronella extract had a significant inhibitory response, demonstrating the potency of essential oils and flavonoid content in preventing the growth and death of bacteria (Hasibuan, G, P, Hutagalung, & Erawati, 2021).

CONCLUSIONS AND RECOMMENDATIONS

While the highest inhibition zone was 60%, the minimum inhibitory content (MIC) and minimum inhibitory content (MBC) of ginger extract (*Zingiber O. Rosc*) on the development of *Porphyromonas gingivalis* ATCC®33277TM concentrations of 10% and 40% (22,87 mm). The efficacy of ginger extract against *Porphyromonas gingivalis* ATCC®33277TM increases with its concentration.

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